

Appl. No. : 08/807,500
 Filed : February 27, 1997

AMENDMENTS TO THE CLAIMS

1. (Cancelled)
2. (Cancelled)
3. (Previously presented) The first nucleotide sequence according to claim 10, wherein the second nucleotide sequence comprises the nucleotide sequence of a oncospecific autonomous parvovirus which is chosen from the group consisting of parvovirus H1, fibrotropic parvovirus variant of Minute virus of Mice (MVMp) and parvovirus LuIII.
4. (Previously presented) The first nucleotide sequence according to claim 10, wherein the second nucleotide sequence comprises a nucleotide sequence of an oncospecific autonomous parvovirus which lacks nucleotide sequences encoding the parvovirus capsid proteins VP1 and VP2.
5. (Previously presented) The nucleotide sequence according to claim 4, further comprising inserted between a promoter P4 and a non-structural protein NSI, a promoter which is activated in target cells.
6. (Previously presented) The nucleotide sequence according to claim 4, wherein the nucleotide sequence of the oncospecific autonomous parvovirus further lacks a nucleotide sequence of a promoter P38 and nucleotide sequences encoding the parvovirus nonstructural proteins NSI and NSII.
7. (Previously presented) The first nucleotide sequence according to claim 10, wherein said third nucleotide sequence comprises an effector nucleotide sequence which comprises at least two coding nucleotide sequences, at least two non-coding nucleotide sequences, or combinations thereof, operably linked in polycistronic subunits under the control of a single promoter unit.
8. (Original) The nucleotide sequence according to claim 7, wherein the effector nucleotide sequence is between two coding nucleotide sequences and the effector nucleotide sequence comprises one IRES nucleotide sequence.
9. (Previously presented) The first nucleotide sequence according to claim 10, wherein the third nucleotide sequence comprises an effector nucleotide sequence which encodes at least one fusion polypeptide containing at least one ligand selected from the group consisting of a hypervariable end of an antibody, a cytokine and a growth factor, wherein the ligand binds specifically to at least one molecule expressed at the surface of cancerous or infected cells.

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10. (Previously presented) A first nucleotide sequence comprising a second nucleotide sequence and a third nucleotide sequence, said second nucleotide sequence comprising the nucleotide sequence of an oncoselective autonomous parvovirus, and said third nucleotide sequence comprising at least one effector nucleotide sequence encoding an effector polypeptide, wherein said effector polypeptide effects the destruction or the normalization of cancer cells,

wherein the effector nucleotide sequence comprises at least one sequence chosen from the group consisting of:

- a nucleotide sequence that encodes a cytotoxic polypeptide or at least one fragment of this polypeptide,
- a nucleotide sequence that encodes a molecule which confers on a transfected cell sensitivity to a radioactive toxic agent,
- a nucleotide sequence that encodes at least one polypeptide which increases an immune response, and
- a nucleotide sequence that encodes at least one polypeptide or a fragment of this polypeptide which inhibits tumor neoangiogenesis.

11. (Previously presented) The first nucleotide sequence according to claim 10, wherein the fragment of the cytotoxic polypeptide encoded by said effector nucleotide sequence is fragment A of diphtheria toxin.

12. (Previously presented) The first nucleotide sequence according to claim 10, wherein the molecule encoded by the effector nucleotide sequence is Herpes simplex virus type 1 thymidine kinase (HSV-TK), and the radioactive toxic agent is a guanosine analog labeled with a radioisotope which emits Auger electrons.

13. (Previously presented) The first nucleotide sequence according to claim 10, wherein the polypeptide which inhibits tumor neoangiogenesis is selected from the group consisting of interferon- α , interferon- β and platelet factor 4.

14. (Previously presented) The first nucleotide sequence according to claim 10, wherein the effector nucleotide sequence comprises at least one nucleotide sequence which can be transcribed into an RNA, which destroys or normalizes cancer cells or infected cells.

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15. (Previously presented) The nucleotide sequence according to claim 14, wherein the nucleotide sequence which can be transcribed into an RNA which destroys or normalizes cancer cells or infected cells is an antisense RNA or a ribozyme.

16 (Previously presented) The first nucleotide sequence according to claim 10 which further comprises at least one regulatory nucleotide sequence activated by transactivation factors specific for a medical condition and/or for the affected cellular tissue and which inactivates the effector nucleotide sequence.

17.-20 (Cancelled)

21. (Currently amended) The nucleotide sequence according to claim 16, wherein the regulatory nucleotide sequence contains at least one promoter and/or at least one enhancer transactivatable in certain specific tissues and chosen from the group consisting of:

-the a nucleotide sequence controlling the expression of the gene encoding α -fetoprotein (AFP),

-the a nucleotide sequence controlling the expression of human placental protein 11 (PP11),

-the a nucleotide sequence controlling the expression of antigen CO-029,

-the a nucleotide sequence controlling the expression of antigen H23,

-the a nucleotide sequence controlling the prostatic expression of prostatic secretory protein PSP94,

-the a nucleotide sequence controlling the expression of the protein pHGR11 associated with melanoma, ovarian cancer, adenocarcinoma of the colon and of the prostate,

-the a nucleotide sequence controlling the expression of protein pHGR74, expressed in the testicles, the prostate, the seminal vesicle and the granulosa of the ovary,

-the nucleotide sequences controlling the expression of proteins specific for the mammalian epithelium,

-the a nucleotide sequence controlling the expression of tyrosinase, expressed in the melanocytes and malignant melanoma,

-the nucleotide sequences controlling the expression of elastase, expressed only in the exocrine pancreas,

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--the a nucleotide sequence controlling the hypophysial expression of prolactin,
and/or

-a mixture thereof.

22. (Previously presented) A recombinant vector comprising the sequence or a portion of the first nucleotide sequence according to claim 10.

23.-27 (Cancelled)

28. (Previously presented) A nucleotide sequence comprising the nucleotide sequence of an autonomous parvovirus, and at least one effector nucleotide sequence encoding a polypeptide which effects the destruction or normalization of cells infected by intracellular infectious parasites,

wherein the effector nucleotide sequence comprises at least one sequence selected from the group consisting of:

-a nucleotide sequence that encodes a cytotoxic polypeptide or at least one fragment of this polypeptide,

-a nucleotide sequence that encodes a molecule which confers on a transfected cell sensitivity to a radioactive toxic agent, and

-a nucleotide sequence that encodes at least one polypeptide which increases an immune response.

29. (Previously presented) The nucleotide sequence of Claim 21, wherein said mammalian epithelium is uterine epithelium.

30. (Previously presented) The nucleotide sequence of Claim 12, wherein said radioisotope is ¹²³Iodine.